REMARKS

Claims 61, 71, 72, 74, 77-79, 81, 85-89 and 92-93 are pending and under examination.

Regarding 35 U.S.C. § 112, First Paragraph (Enablement)

Applicants respectfully traverse the rejection of claims 61, 71, 72, 74, 81, 85 and 86 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Applicants respectfully maintains that the specification enables the full scope of the claimed invention for the reasons that follow.

The test for enablement is whether one skilled in the art could make and use the claimed invention from the disclosure coupled with information known in the art without undue experimentation. *See United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343, 1345 (CCPA 1976). In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure).

Applicants respectfully submit that the examiner has not met the initial burden to establish a reasonable basis to question the enablement. The current Office Action (mailed February 2, 2010), at page 3, alleges the following:

> It is art known that the complement system comprises a multitude of proteins circulating in blood plasma, hence the complement system and its component exists in normal individuals as well as those that my have breast cancer.

The Office Action reasons that SEQ ID NO:1320 would be detected in both, cancerous and non-cancerous patient samples given the ubiquitous nature of CR1. Current Office Action, page 4. Applicants respectfully submit that whether or not CR1 is present in both cancerous and non-cancerous tissues is not relevant to the issue of enablement of the claimed methods. In particular, while the independent claims are directed to disgnostic methods that require detection of differential expression of CR1 between two tissues, there is no requirement that CR1 is present in one of the tissues and not expressed at all in the other. Rather, one skilled in the art would appreciate that differential expression merely requires a measurable difference in the

expression levels between the two tissues. CR1 expression that is "ubiquitous" does not preclude differential expression levels between cancerous and non cancerous tissues and "all-versus-none" CR1 expression is not a prerequisite to practice the claimed diagnostic methods. Accordingly, the examiner has not met the initial burden to establish a reasonable basis to question the enablement.

In view of the above, Applicants respectfully request removal of the rejection of claims 61, 71, 72, 74, 81, 85 and 86 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

Regarding 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 61, 71, 72, 74, 77-79, 81, 85, 91 and 92 under 35 U.S.C. § 102(b) as allegedly being anticipated by Qi et al., Abstract from British Journal of Cancer 69(5): 903-910, 1994). The Examiner alleges that Qi et al. discloses the increased expression (82%) of cripto-1 (CR-1) primary infiltrating ductal (IDCs) and infiltrating lobular breast carcinomas (ILCs) examined immunocytochemistry. According to the Examiner, absent evidence to the contrary the CR-1 described in Qi et al. is the same as the CR1 corresponding to SEQ ID NO: 1320 in the claimed invention. **Cripto-1 (CR-1)** is a glycosylphosphatidylinositol (GPI)-anchored membrane glycoprotein that has been shown to play an important role in embryogenesis and cellular transformation. *See* Watanabe et al., *J. Biol. Chem.*, 282(43):31643-31655 (2007), attached hereto as Attachment A. The rejected claims recite methods encompassing the **complement receptor type 1 (CR1)** gene, which encodes a single pass transmembrane glycoprotein that, through its ability to bind key components of the complement cascade, can inhibit both the classical and alternative pathways. **Cripto-1 (CR-1) and complement receptor type 1 (CR1) are distinct proteins encoded by distinct genes.** The claims recite SEQ ID NO. 1320, a nucleotide sequence. Translating SEQ ID NO. 1320 into a polypeptide sequence provides a sequence identical to SEQ ID NO. 1321 as disclosed in the specification. Using either the translated SEQ ID NO. 1320 or SEQ ID NO. 1321 and aligning it with the Cripto-1 polypeptide as disclosed by the cited references shows that the polypeptides are of significantly differing length (474 v. 188) and have only 14.5% homology. Attached as Attachment B is a PDF document with the polypeptide alignments. Attached as Attachment C is a Word document with polypeptide alignments, polypeptides sequences used in the alignments, a nucleotide alignment and the nucleotide sequences used in

the alignment. Applicants respectfully request removal of the rejection of claims 61 , 71 , 72 , 74, 77- , 81 , 85, 91 and 92 under 35 U.S.C. § 102(b) as allegedly being anticipated by Qi et al., Abstract from *British Journal of Cancer* 69(5): 903-910 (1994).

Applicants respectfully traverse the rejection of claims 91 and 92 under 35 U.S.C. § 102(b) as allegedly being anticipated by Saeki et al., *Cancer Research* 52:3467-3473 (1992). Saeki allegedly discloses increased expression of cripto in human colorectal tumors in contrast to no expression of cripto in normal colon specimens. As described in more detail above, Cripto-1 (CR-1) and complement receptor type 1 (CR1) are distinct proteins encoded by distinct genes. Applicants respectfully request removal of the rejection of claims 91 and 92 under 35 U.S.C. § 102(b) as allegedly being anticipated by Saeki et al., *Cancer Research* 52:3467-3473 (1992).

Applicants respectfully traverse the rejection of claims 61, 71, 72, 74, 77-79, 81, 85, 86, 91 and 92 under 35 U.S.C. §102(e) as being anticipated by U. S. Patent Application Publication number 2004/0054142 A1 (effective filing date August 4 2003). The Examiner alleges that the cited patent publication discloses diagnosing lung, colon and breast cancer with the assessment of cripto tumor polynucleotides and polypeptides via RT-PCR. As described in more detail above, Cripto-1 (CR-1) and complement receptor type 1 (CR1) are distinct proteins encoded by distinct genes. Applicants respectfully request removal of the rejection of claims 61, 71, 72, 74, 77-79, 81, 85, 86, 91 and 92 under 35 U.S.C. § 102(e) as allegedly anticipated by U. S. Patent Application Publication number 2004/0054142 A1 (effective filing date August 4 2003).

Regarding 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Qi et al., Abstract from *British Journal of Cancer* 69(5): 903-910 (1994), and further in view of U. S. Patent Application Publication number 2004/0054142 A1 and U. S. Patent 6,852 506. As set forth herein, the primary reference is directed to Cripto-1 (CR-1). As described in more detail above, Cripto-1 (CR-1) and complement receptor type 1 (CR1) are distinct proteins encoded by distinct genes. Accordingly, Qi et al., whether viewed alone or in combination with U. S. Patent Application Publication number 2004/0054142 A1 and U. S. Patent 6,852 506, does not teach or suggest the claimed methods reciting complement receptor type 1 (CR1). Applicants respectfully respectfully request removal of the rejection of claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Qi et al., Abstract from *British*

Journal of Cancer 69(5): 903-910 (1994), and further in view of U. S. Patent Application Publication number 2004/0054142 A1 and U. S. Patent 6,852 506.

Applicants respectfully traverse the rejection of claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U. S. Patent Application Publication number 2004/0054142 in view of U. S. Patent 6,852 506. As set forth herein, the primary reference is directed to Cripto-1 (CR-1). As described in more detail above, Cripto-1 (CR-1) and complement receptor type 1 (CR1) are distinct proteins encoded by distinct genes. Accordingly, U. S. Patent Application Publication number 2004/0054142 A1, whether viewed alone or in combination with U. S. Patent 6,852 506, does not teach or suggest the claimed methods reciting complement receptor type 1 (CR1). Applicants respectfully respectfully request removal of the rejection of claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U. S. Patent Application Publication number 2004/0054142 A1, and U. S. Patent 6,852 506.

Regarding Nonstatutory Obviousness-Type Double Patenting

Claims 61, 71, 72, 74, 77-79, 81 and 85-89 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 42, 43, 44 and 49 of co-pending USSN 10/573,332 (filed April 6 , 2007). Because this rejection is provisional and neither set of the allegedly conflicting claims has been allowed or patented, Applicants respectfully request deferral of this ground of rejection until there is an indication of allowable subject matter in one or both applications.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned attorney if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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